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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,335	12/12/2003	Doddabele L. Madhavi	BIO 2-016	3791

266 7590 10/13/2006

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EXAMINER

MAIER, LEIGH C

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/735,335

Applicant(s)

MADHAVI ET AL.

Examiner

Leigh C. Maier

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 July 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/03/6</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

Claims 1-20 have been amended and are pending. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Any objection or rejection not expressly repeated has been withdrawn.

Claim Rejections - 35 USC § 102

Claims 1-3 and 5 are again rejected under 35 U.S.C. 102(b) as being anticipated by Szente et al (J. Incl. Phen., 1998), as set forth in the previous Office action.

Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive.

Applicant goes on at length about the variables regarding cyclodextrin complexation and the differences in various carotenoids. While this is interesting, it is not relevant to the claims at hand.

Applicant further contends that complexation with cyclodextrins "often" may not result in increased bioavailability. However, the instant issue is the product disclosed by Szente. It is not required to have increased bioavailability with respect to anything. It is only required to be "bioavailable."

Applicant also notes the differences in products described by Szente. Again, not relevant. The differences have nothing to do with whether or not the disclosed product meets the limitations of the instant claims.

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Applicant states that the Szente complexes are ternary complexes of three components, whereas the present application describes a product having no complexation between the oil and the cyclodextrin. First of all, the examiner does not find any description of a product stating that there is no complexation between the oil and the cyclodextrin. Furthermore, the examiner finds no limitation in the claims precluding said complexation.

Applicant again notes the differences in the spray-dried and freeze-dried products in the working example. However, what is being claimed is a product in oil. As in seen in Szente, the oil interacts with the cyclodextrin and may affect the in vivo properties of the complexes.

Applicant further notes that a composition and its properties are inseparable. The examiner agrees and for this reason maintains that the product of Szente appears to meet the physical limitations of the claims. The burden is on Applicant to demonstrate with evidence, not arguments, that the art product is different from that of the claims.

Claims 1, 2 and 5-7 are again rejected under 35 U.S.C. 102(b) as being anticipated by Basu et al (JAOCS, 2001), as set forth in the previous Office action.

It is noted that the remarks submitted in response to the previous Office action comprise three sections: (1) Summary of the claim rejections; (2) Summary of the cited art; and (3) The rejection of the claims, or what appears to be the arguments in response to the rejection of the claims. In this last section, there is no specific argument with respect to the rejection over Basu. Therefore, the examiner is taking the discussion of Basu in section (2) and the alleged differences as the traversal of the rejection.

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Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive.

Again, it appears to be Applicant's position that the instant product does not comprise an oil complex with the cyclodextrin, so distinguishing it from the product disclosed by Basu. As noted above, there is no limitation precluding such a complex in the instant product.

Claim Rejections - 35 USC § 103

Claims 1-3 and 5 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Szente et al (J. Incl. Phen., 1998) in view of Hedges (Chem. Rev., 1998), as set forth in the previous Office action.

Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive.

Applicant alleges that Hedges does not teach freeze drying as a common method for drying cyclodextrin complexes and states that this combination "specifically excludes freeze-drying." The examiner respectfully disagrees. Please see the second paragraph under section E. of Hedges, as cited in the previous Office action. Applicant fails to cite the passage that "specifically excludes freeze-drying."

The fact that the claims do not preclude a ternary complex has been addressed above.

Claims 1-3 and 6 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000), as set forth in the previous Office action.

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Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive.

Applicant again cites one of the declarations submitted in this case. This declaration discusses imperfect predictability with respect to cyclodextrin complexation and whether or not a compound so complexed would have increased bioavailability.

Applicant contends that cyclodextrin/carotenoid bonds could be disrupted by a number of factors, including excipients, such as oils, surfactants, phospholipids, etc. This is exactly why the examiner maintains that the example of the cyclodextrin complex tested *without* oil, is not the appropriate test for demonstrating unexpected results. The examiner agrees that these excipients can interact with the cyclodextrin, but there is no teaching of record, that would suggest to one of ordinary skill that they should not be combined, especially since they are all known solubilizers. It appears to be Applicant's position that one of ordinary skill would be motivated to combine elements only in the case where he could predict the result with absolute certainty. Applicant is reminded that perfect predictability is not required for a prima facie case of obviousness.

Applicant notes the difference in recovery (95% for freeze-drying vs. 50% for spray-drying) in the two different drying methods. This might be seen as unexpected results with respect to a method of making claim. However, the examiner finds no such evidence of this difference in the specification of any submitted declarations. Furthermore, these claims are product claims only.

Applicant contends that Olmedilla does not indicate that a cyclodextrin complex of a carotenoid can be formulated for soft gelatin capsules, or that it remains bioavailable after formulation. Indeed, if this were that case, it would have been a rejection based on anticipation

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rather than obviousness. The examiner maintains that in view of the *combination* of references, the one of ordinary skill would reasonably expect success in modifying Olmedilla with the addition of a cyclodextrin.

Applicant further states that Olmedilla does not teach the inter-individual variations in the uptake of lutein from oil dispersions. The examiner fails to see how this is relevant as there appears to be no such functional language in the claims.

Applicant contends that the art of record demonstrate the unpredictable nature of cyclodextrin complexes of carotenoids. However, the cited references appear to be drawn to comparisons of cyclodextrins vs. oil and would have not particular bearing on cyclodextrin + oil. It is further noted that “unpredictable” is not the same as “unexpected.”

Claim 4 is again rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000) as applied to claims 1-3 and 6 above, and further in view of Kulevskaya et al (Pharm. Chem. J., 2002), as set forth in the previous Office action.

Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive.

Applicant cites Baskaran et al and interprets this reference as teaching that lecithin “lower[s] the uptake of carotenoids ... solubilized in mixed micelles by Caco2 cells and animal studies.” However, Applicant omits important information in this characterization. The reference concludes “the hydrolysis of PC (lecithin) to lysoPC plays an important role in the intestinal uptake of carotenoids solubilized in mixed micelles.” See abstract. However, the products were

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administered directly into the stomach, thereby short-circuiting the digestive process and shortening the time during which the hydrolysis might take place. Applicant notes that the data in the specification demonstrate that the uptake of lutein with cyclodextrin/oil/lecithin is improved over that of lutein with oil/lecithin. However, this is what would be expected from the teachings upon which this rejection is based.

Applicant further states that the lutein was not solubilized in the lecithin, but the lecithin was used as an excipient. The examiner is not clear what Applicant feels is the distinction here or how it might limit the claim.

Claims 5 and 7 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000) as applied to claims 1-3 and 6 above, and further in view of Szenté et al (J. Incl. Phen., 1998), as set forth in the previous Office action.

Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive. Applicant does not provide additional arguments not addressed above.

Claim 9 is again rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000) as applied to claims 1-3 and 6 above, and further in view of Sharper (Manufacturing and Formulation, 2001 – retrieved 3/30/06 at <http://www.samedanltd.com/members/archives/PMPS/Autumn2001/PeterSharper.htm>), as set forth in the previous Office action.

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Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive. Applicant does not provide additional arguments not addressed above.

Claims 8 and 10 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000), and further in view of Szente et al (J. Incl. Phen., 1998), as applied to claims 1-3 and 5-7 above, and further in view of Kulevskaya et al (Pharm. Chem. J., 2002) and Sharper (Manufacturing and Formulation, 2001 – see link above.), as set forth in the previous Office action.

Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive. Applicant does not provide additional arguments not addressed above.

Claims 11-13, 15-17 and 19 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000), Sharper (Manufacturing and Formulation, 2001 – see link above) and Mele et al (Carbohydr. Res., 2002), as set forth in the previous Office action.

Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive.

Applicant notes the finding that the cyclodextrin-complexed carotenoid is not stable in a hard capsule, and but it is in a gel capsule. However, it is not just the cyclodextrin-complexed carotenoid in the gel capsule, but the cyclodextrin-complexed carotenoid *in oil* in the gel capsule. The fact that the carotenoid is more stable in the presence of two known stabilizing agents than in the presence of one stabilizing agent is not surprising. Applicant contends that this is contrary

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to Dr. Madhavi's hypothesis that the oil might inhibit the dispersion of the complex, and that this is unexpected. The examiner respectfully disagrees. The fact that this result is not perfectly predictable does not make it unexpected. A synergistic effect, for example, would be unexpected. In order for this to be unexpected, there must be clear and specific reasoning as to why one of ordinary skill would not expect an additive effect in this case.

Claims 14, 18 and 20 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000), Sharper (Manufacturing and Formulation, 2001 – see link above) and Mele et al (Carbohydr. Res., 2002), as applied to claims 11-13, 15-17 and 19 above, and further in view of Kulevskaya et al (Pharm. Chem. J., 2002), as set forth in the previous Office action.

Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive. Applicant does not provide additional arguments not addressed above.

Double Patenting

Claims 1-3 are again provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3 and 9 of copending Application No. 10/309,999.

Applicant's arguments filed July 3, 2006 have been fully considered but they are not persuasive.

Applicant notes that the copending claims have been amended to require a "powder form," and this results in a hydrophilic, water dispersible fine powder. However, claim 3 requires

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the addition of oil, so it is not clear how the product differs from the instant one. The examiner maintains that no unexpected results, with respect to the instant claims, have yet been presented.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

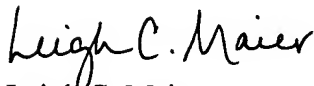
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Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

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Leigh C. Maier
Primary Examiner
September 29, 2006